

# **Exhibit 7**

# Osteoporosis, Calcium and Estrogens

by Roger W. Miller

Osteoporosis is a condition in which bones become weakened. Usually afflicting older people, it results in fractures of the hip, wrist, spine and other bones. Some 1.3 million fractures a year are attributed to the condition.

Women are more prone to osteoporosis than men. Among those who live to be 90, about one out of three women and one out of six men will suffer a hip fracture, most due to osteoporosis. So prevalent is the problem among women that a condition in which the spinal bones become so weak they literally collapse, leaving a hunched back, has become known as "dowager's hump." Such a condition can rob a woman of 2 to 8 inches in height.

In osteoporosis, the weakening of the bones is due to a loss of bone mass or density. A shortage of calcium is one reason for this loss. Another is a lack of the hormone estrogen. Body levels of estrogen decline during menopause, and the resultant bone mass loss continues three to seven years after.

But estrogen loss is not the only reason that four times as many women as men over 55 suffer bone fractures. Women start out with 30 percent less bone mass than men. This is particularly true of Caucasian women, making osteoporosis more of a problem for whites than blacks.

Osteoporosis was the subject of a consensus conference at the National Institutes of Health (NIH) in April 1984. Conference experts agreed on the need for more calcium in the diet as well as the possibility that some women require extra doses of estrogen.

Stepping up calcium intake may also mean a need for more vitamin D, which is required for optimal calcium absorption. The vitamin D link is particularly important because



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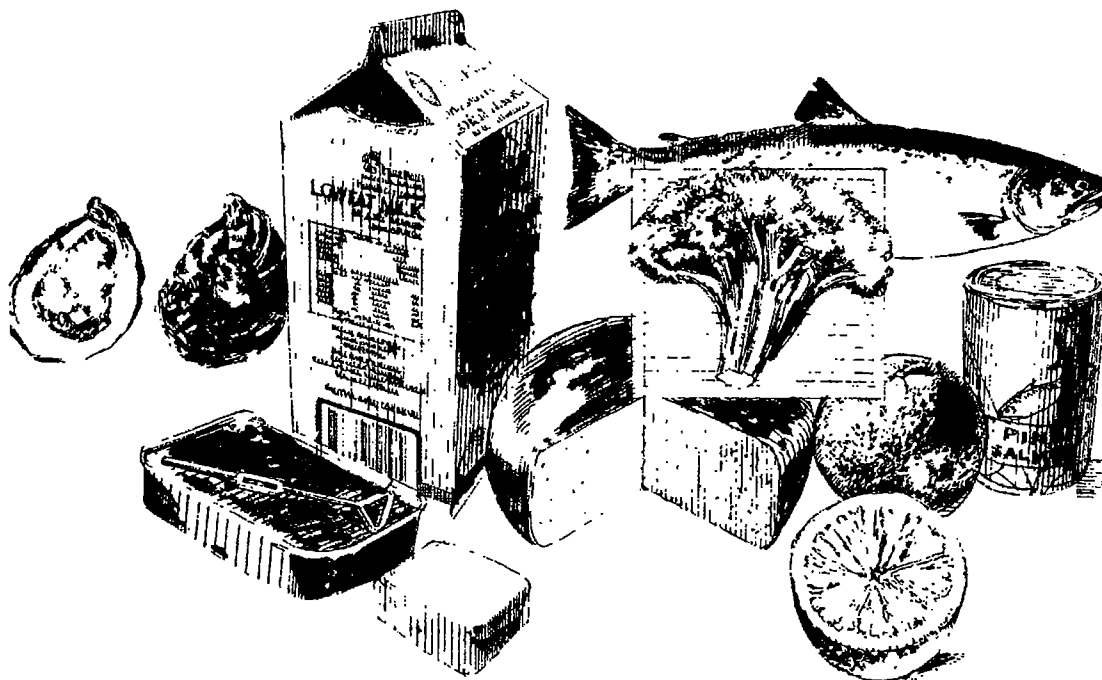
### Adult Calcium Consumption

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**Estimated actual intake** 450-550 mg daily

**U.S. Recommended Daily Allowance (USRDA)** 1,000 mg daily

**Recommended by osteoporosis consensus conference experts for post-menopausal women** 1,500 mg daily



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as people get older their intestines may not absorb calcium as well.

The conferees said that smoking and alcohol contribute to osteoporosis. On the other hand, they agreed that exercise could help prevent bone loss, and they endorsed "modest weight-bearing exercise," such as walking.

The NIH conference findings were based on much research that has been conducted over the years. One of the researchers, Dr. Hunter Heath III of the Mayo Clinic, Rochester, Minn., summed up the situation in the June 1983 issue of *The Annals of Internal Medicine*: "Not entirely in jest, the person at grave risk of postmenopausal osteoporosis may be pictured as a slender 5 foot 2 inch, blue-eyed woman who works behind a desk, smokes a pack a day, enjoys her cocktail before steak, and abjures milk."

The size of Dr. Heath's candidate is a reference to women of smaller stature having less overall bone mass than their larger counterparts.

Bones contain 99 percent of the calcium in the body. The other 1 percent is found in the blood and other body fluids where, among other things, it helps in blood clotting and nerve transmission. (See "Calcium: More Than Just The Strong Stuff Of Bones" in the July-August 1981 *FDA Consumer*.) Calcium is stored in the bones and drawn upon when the daily intake isn't enough to meet the body's needs.

The U.S. Recommended Daily Allowance for calcium is 1,000 milligrams (mg) for adults. However, the consensus conference said that actual intake for adults is only 450 to 550 mg a day, and that women who have passed menopause may need as much as 1,500 mg daily.

Milk and other dairy products, fish

with bones (such as canned salmon and sardines), oranges, leafy green vegetables (such as collards and turnip greens) and broccoli are among the major sources of calcium. A cup of lowfat yogurt contains 350 to 450 mg of calcium, while a cup of skim milk has 300 to 350 mg. A half cup of ice cream and an ounce of mozzarella cheese offer 100 and 150 mg respectively. Those figures indicate that getting up to 1,500 milligrams a day may be no easy task, particularly for people who do not regularly consume such calcium-rich products.

As a result, some experts are recommending calcium supplements for older women. The consensus conference went a step further, recommending that the calcium intake be increased "well before the menopause."

However, a couple of words of caution have been voiced about calcium supplementation. Some people form urinary tract (kidney) stones. Anyone with a history of kidney stones should consult a physician before using calcium supplements.

The second caution concerns the source of calcium. Some people take bonemeal and dolomite (a rock mineral source) for additional calcium. But FDA warned in its April 1982 issue of the *Drug Bulletin* that the two products may contain lead in amounts that would constitute a risk for infants, children, women of childbearing age, and possibly the elderly.

Calcium supplements are readily available in supermarkets and drugstores, and the market is growing rapidly. In February 1984, nearly two months before the NIH conference, both *Advertising Age* and *The Wall Street Journal* ran articles on the growing calcium supplement market

and the producers' plans, now evident, to advertise their products to the public. Previously, their advertisements had been limited mostly to medical and other health professional publications.

Vitamin D, which helps in calcium absorption, also is found in milk and other products to which vitamin D has been added. In addition, it's available free from the sun. If dietary supplements containing vitamin D are used, they should not exceed the Recommended Daily Allowance of 400 IU (international units) because continued use of high doses has toxic effects.

Growing along with calcium supplement sales is the market for oral estrogen drugs, although a prescription is required to obtain these. The dominant estrogen pill maker had a 6 percent sales gain in the first seven months of 1984.

FDA's Fertility and Maternal Health Drugs Advisory Committee has recommended a labeling change for estrogens that would include their use for prevention and treatment of osteoporosis. The committee also recommended retention of the boxed warning on estrogen labels about the reported increased risk of endometrial (lining of the uterus) cancer faced by women who receive estrogen therapy. The consensus conferees noted that estrogen-associated endometrial cancer "is usually manifested at an early stage and is rarely fatal when managed appropriately."

Estrogen therapy also has raised some concern about breast cancer, but both the NIH experts and the FDA advisory group said the bulk of evidence didn't back up such a link. ■

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